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Treatment of Gram-Negative Septic Shock with Human IgG Antibody to *Escherichia coli* J5: A Prospective, Double-Blind, Randomized Trial

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In a randomized, double-blind, multicenter trial we compared the efficacy of a preparation of human IgG antibody to *Escherichia coli* J5 (J5-IVIG) with that of a standard IgG preparation (IVIG) for the treatment of gram-negative septic shock. At study entry, patients received a single intravenous dose of 200 mg/kg of body weight (maximal dose, 12 g) of either J5-IVIG or IVIG. Of the 100 patients randomized, 71 (30 receiving J5-IVIG and 41 receiving IVIG) had a documented gram-negative infection. Mortality from gram-negative septic shock was 50% (15 of 30) in J5-IVIG recipients and 49% (20 of 41) in IVIG recipients. In addition, treatment with J5-IVIG did not reduce the number of systemic complications of shock and did not delay the occurrence of death due to septic shock. Thus we conclude that J5-IVIG was not superior to IVIG in reducing mortality or in reversing gram-negative septic shock.

Episodes of gram-negative bacteremia are associated with a death rate of 20%–30% [1–3], but in patients developing septic shock, fatality ratios are in the range of 50%–80% [4]. Because advances in antimicrobial therapy have not had a major impact on lowering the lethality of septic shock, other therapeutic approaches have been investigated, such as passive immunotherapy with antiserum to the lipopolysaccharide (LPS) or endotoxin core of gram-negative bacteria or treatment with corticosteroids or opiate antagonists. However, despite successes in animal models [5–10], well-designed clinical trials using either high-dose corticosteroids or naloxone have failed to demonstrate an increased survival of patients with septic shock [11–14].

The concept of passive immunotherapy with antiserum to the endotoxin core of gram-negative bacteria relies on the following considerations. Among gram-negative bacteria, the central part of the LPS (the core glycolipid, which is made up of lipid A and the core oligosaccharide) is a highly conserved struc-

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This trial was conducted in accordance with the guidelines laid down in the Declaration of Helsinki and was approved by the Human Subjects and Ethics Committees of the participating centers. Depending on the patient's clinical condition, the informed consent was given either by the patient or by the physician in charge of the patient.

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